REMARKS

Claims 1-18 are pending in the present application and claims 11-12 and 19-50 are currently withdrawn from consideration. Claims 1 and 3 have been amended. Claims 2 and 4-6 have been canceled, without prejudice. Support for the amendments may be found throughout the specification, including the claims as originally filed. Applicants will also cooperate with the Examiner's request to correct any errors in the specification of which Applicants may become aware.

Amendment or cancellation of claims should not be construed as an acquiescence, narrowing, or surrender of any subject matter. The amendments are being made not only to point out with particularity and to claim the present invention, but also to expedite prosecution of the present application. Applicants reserve the right to prosecute the originally filed claims further, or similar ones, in the instant or subsequently filed patent applications.

Objections to the Specification

The Examiner has objected to the use of the trademarks PLURONIC and FICOLL on page 34, line 17 and on page 43, line 19, respectively, of the specification. Applicants have amended the specification to designate the proprietary nature of the marks. Applicants therefore respectfully request withdrawal of the objection.

Rejection under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 1-10 and 13-18 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner contends that there is insufficient disclosure in the specification where "[t]he instant claims encompass an MHC class II compound comprising any spaceholder molecule of any sequence, and not necessarily a CLIP peptide or substitution variant thereof capable of binding in the peptide binding groove, and including the spaceholder molecule that has, i.e., comprises, the poly-Ala peptide recited in instant claim 10." More specifically, the Examiner states that "[s]ince the disclosure fails to provide sufficient relevant identifying characteristics, and because the genus is highly variant, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus as broadly claimed."

Applicants respectfully traverse the rejection. However, in an effort to expedite prosecution, Applicants have amended claim 1 to recite spaceholder molecules with low or intermediate binding affinity. Support for this amendment can be found throughout the specification as filed, including at page 4, line 12-25 and page 15, lines 28-30. Moreover, Applicants disclose representative examples of spaceholder molecules including SEQ ID NOS: 1-5 and 36, as well as specific, non-limiting examples of binding affinities for these spaceholder molecules (see, for example, Example 1B). It is therefore Applicants' position that the specification provides sufficient defining characteristics of the claimed genus of spaceholder molecules. Accordingly, applicants respectfully request withdrawal of the rejection.

Rejection under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claims 4-6 and 11-12 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Specifically, the Examiner has rejected claim 4 as allegedly being indefinite in the recitation of "wherein said spaceholder molecule binds covalently to said peptide binding groove." The Examiner states that "it is not clear what is meant, i.e., if the spaceholder molecule is covalently attached to one of the MC class II chains, or if there are moieties within the spaceholder molecule that make covalent attachments to the amino acid residue side chains of amino acid residues within or lining the peptide binding groove of the MHC class II molecule." In an effort to expedite prosecution, Applicants have canceled claim 4 without prejudice, and therefore believe that the rejection is rendered moot. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

The Examiner has also rejected claim 11 as allegedly being indefinite in the recitation of "AAMAAAAAAAMAA (SEQ ID NO:2)." The Examiner states that "it is not clear what is meant, i.e., the recited sequence is 13 amino acid residues in length whereas SEQ ID NO:2 in the sequence listing filed 7/11/03 is 12 amino acid residues in length." Applicants respectfully submit that the correct sequence for SEQ ID NO:2 (including 13 amino acids) was disclosed in the application as filed on page 4, lines 21-22; page 16, lines 3-4; and claim 41. Accordingly, Applicants submit herewith a corrected Sequence Listing reciting the correct sequence for SEQ

ID NO:2, as disclosed in the specification. Applicants submit that no new matter has been added. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Rejection under 35 U.S.C. § 102

The Examiner has rejected claims 1-9, 13, and 16-18 under 35 U.S.C. § 102(b) as allegedly being anticipated by Scott et al. (J. Exp. Med. 1996, 183: 2087-2095, IDS reference) as evidenced by Kozono et al. (Nature, 1994, 369: 151-154, IDS reference). The Examiner asserts that "Scott et al. teach a soluble IA molecule (i.e., the extracellular domains of the α and β chains of an MHC class II) wherein an ***antigenic peptide*** sequence, i.e., a spaceholder molecule that binds in the peptide binding groove, is added to the amino terminus of the class II β chain, and wherein the soluble IA molecule comprises leucine zipper peptides linked by a thrombin sensitive cleavage site to the class II chains, i.e., an effector component linked to the MHC class II α chain by a second linker. Scott et al. teach that the strategy of fusing peptide residues that correspond to the antigenic peptide sequence to the amino terminus of the β chain of class II MHC has been recently described by Kozono et al. in reference #5."

Applicants respectfully traverse the rejection. A claim is only anticipated if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference (MPEP 2131). Scott et al. does not teach or suggest each and every element of the claimed invention, i.e., the use of a spaceholder molecule, wherein said ***spaceholder molecule binds with intermediate or low affinity*** as claimed in amended claim 1 and dependent claims thereof. Therefore, Scott et al. does not anticipate the claimed invention. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

The Examiner has also rejected claims 1-5, 7-9 and 14 under 35 U.S.C. § 102(b) as allegedly being anticipated by Kozono et al. (Nature, 1994, 369: 151-154, IDS reference). The Examiner states that "Kozono et al. teach an MHC class II compound comprising the extracellular domains of the α and β chains of MHC class II, and a peptide attached by a flexible peptide linker to the amino terminus of the MHC class II β chain and including a thrombin sensitive cleavage site, wherein the peptide is a ***13-mer peptide that binds well*** to the binding groove formed by the MHC class II chains, said compound being immobilized by an anti-β chain

monoclonal antibody or absorbed to tissue culture plate wells, i.e., the MHC class II component is linked to the effector component."

Applicants respectfully traverse the rejection. Kozono et al. does not teach or suggest each and every element of the claimed invention, i.e., the use of a ***spaceholder molecule, wherein said spaceholder molecule binds with intermediate or low affinity*** as claimed in amended claim 1 and dependent claims thereof. Therefore, Kozono et al. does not anticipate the claimed invention. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

The Examiner has rejected claims 1 and 4-9 under 35 U.S.C. § 102(b) as allegedly being anticipated by Zhong et al. (J. Exp. Med. 1996, 184: 2061-2066). The Examiner asserts that "Zhong et al. teach an MHC class II compound comprising the MHC class II α chain and the MHC class II β chain, the β chain linked to the mouse Ii 89-100 invariant chain CLIP peptide via a linker, and the compound further associated with a chemical dye on SDS-PAGE or associated with a radiolabel upon metabolic labeling, i.e., associated with an effector component."

Applicants respectfully traverse the rejection. Zhong et al. does not teach or suggest each and every element of the claimed invention, i.e., the use of a spaceholder molecule, wherein said ***spaceholder molecule is linked to the claimed MHC class II by a processable linker*** as claimed in amended claim 1 and dependent claims thereof. Therefore, Zhong et al. does not anticipate the claimed invention. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. § 103

The Examiner has rejected claims 1 and 4-12 under 35 U.S.C. § 103(a) as being unpatentable over Zhong et al. (J. Exp. Med. 1996, 184: 2061-2066) in view of Malcherek et al. (J. Exp. Med. 1995, 181: 527-536, IDS reference) and DiBrino et al. (J. Biol. Chem. 1994, 269(51): 32426-32434). Specifically, the Examiner states that "[i]t would have been prima facie obvious to one of ordinary skill in the art at the time the invention as made to have extended the amino terminus of the CLIP 105-117 peptide out sequentially (as well as the carboxy terminus), including making a peptide with the sequence PVSKMRMATPLLMQA (amino acid residues 103-117), in order to determine if binding fully commensurate with the CLIP 97-120 peptide

could be obtained, and to have made a construct of the structure taught by Zhong et al. but using a human HLA class II molecule such as HLA-DR17 taught by Malcherek et al. that binds the CLIP 105-117 and the CLIP 97-120 peptide, and the extended peptides such as CLIP 103-117." The Examiner further asserts that "DiBrino et al. teach making poly-Ala peptides having residues deemed important for binding to an MHC molecule as well as performing an Ala scan on a peptide to study the contribution of each said residue for binding" and that "[i]t would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have made a peptide with the sequence AAMAAAAAAMAA, AAFAAAAAAAAAA, or AAMAAAAAAAAAA, i.e., one having the two residues deemed important by Malcherek et al., or one having the Met 107 deemed important for binding to HLA-DR4w4, or one with a Phe substituent for Met 107 that improves binding of the parental peptide as taught by Malcherek et al., and to have made a construct such as taught by Zhong et al. for mouse."

Applicants respectfully traverse the rejection. Applicants respectfully submit that the references must be viewed as a whole and must suggest the desirability of the claimed invention without the benefit of impermissible hindsight reconstruction afforded by the claimed invention. Furthermore, in order "[t]o establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." MPEP §2143.03 citing *In re* Royka, 490 F.2d 981, 180 USPQ 580 (CCPA 1974).

Neither Zhong et al., Malcherek et al., nor DiBrino et al., either alone or in combination, teach or suggest each and every element of the claimed invention, i.e., ***a spaceholder molecule of the claimed invention that is linked with a processable linker to an MHC class II component of the invention***, as recited in amended claim 1 and dependent claims thereof. Therefore, the combination of references fails to teach the claimed invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

The Examiner has rejected claims 1-18 under 35 U.S.C. § 103(a) as being unpatentable over Scott et al. (J. Exp. Med. 1996, 183: 2087-2095, IDS reference) in view of Kozono et al. (Nature, 1994, 369: 151-154, IDS reference) and Crawford et al. (Immunity. 1998, 8: 675-682, IDS reference). Specifically, the Examiner contends that "[i]t would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have multimerized the complexes taught by Scott et al., plus or minus the leucine zipper peptides,

using the methodology of Crawford et al." The Examiner further alleges that "[o]ne of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to increase the avidity of reactivity of the complexes with T cells as taught by Crawford et al."

Applicants respectfully traverse the rejection. Neither Scott et al., Kozono et al., nor Crawford et al., teach or suggest each and every element of the claimed invention, i.e., the use of a spaceholder molecule, wherein said ***spaceholder molecule binds with intermediate or low affinity*** as claimed in amended claim 1 and dependent claims thereof. Therefore, the combination of references fails to teach the claimed invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

CONCLUSION

Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at (617) 832-1000. If any fees are due, the Commissioner is hereby authorized to credit any overpayment or charge any deficiencies to Deposit Account No. **Deposit Account No. 06-1448, Reference No. DFS-044.01.**

Respectfully submitted,

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Dated: June 20, 2007

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